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SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL EVALUATION OF 4-(4-BROMO-1-HYDROXYNAPHTHALEN-2-YL)-6-ARYL-5,6-DIHYDROPYRIMIDIN-2(1H)-ONE

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ABSTRACT

1-(4- Bromo -1-hydroxynaphthalen-2-yl)-ethan-1-one was prepared by refluxing 4- bromonaphthalen-1-ol with glacial acetic acid in presence of fused $ZnCl_2$. By condensing 1-(4- bromo -1-hydroxynaphthalen-2-yl)-ethan-1-ones with aromatic aldehydes, 1-(4- bromo -1-hydroxynaphthalen-2-yl)-3-aryl-prop-2-en-1-one were synthesized. 1-(4- Bromo -1-hydroxy-naphthalen-2-yl)-3-aryl-prop-2-en-1-ones, urea and concentrated HCl in DMF were added and refluxed. Cool and pour in crushed ice. Treat it with cold NH_4OH solution to obtain titled compounds. The compounds thus synthesized have been characterized by physical and spectral data. All of these titled synthesized compounds have been screened for antimicrobial study and are found to posses excellent antimicrobial activities.

KEYWORDS: antimicrobial activities, cold NH_4OH solution, concentrated HCl in DMF.

INTRODUCTION

In recent scenario heterocycles play a major role in drug synthesis. Heterocyclic compounds like pyrazoles, pyrazolines, thiazoles, dihydropyrimidin-2-one etc having excellent antimicrobial and antifungal activities.[1-4]

Dihydropyrimidin-2-one derivatives shows variety of pharmacological activities such as active and safe tumor anti-initiating and multi-potent blocking agent[5], potential calcium channel blockers[6], analgesic activity[7], anti-microbial activities[8, 9], antihypertensive agents[10], antifilarial agents[11] antioxidant agents[12] vitro anticancer activity.[13]

Synthesis characterization and biological evaluation of titled compound becomes favorate field for many investigator. Their efforts are quite significant in literature. Hence, Considering the scope of pyrimidine derivatives we have synthesized novel 4-(4-bromo-1-hydroxynaphthalen-2-yl)-6- aryl-5, 6-dihydropyrimidin-2(1H)-one compounds from 4-bromo-naphthalen-1-ol and studied for their biological activities.

MATERIALS AND METHODS

The melting points (ºC) were recorded by open capillary method and are uncorrected. IR spectra (υ max in cm-1) were recorded on a Shimadzu FTIR 8300 spectrophotometer using KBr pellets. The 1H NMR spectra were recorded on DRX-300 (300 MHZ) instrument using $CDCl_3$ as solvent (chemical shift in δppm) and TMS as internal standard. Thin Layer Chromatography on silica gel-G, was used to check the purity of the compounds.

METHOD AND DISCUSSION OF RESULT

Synthesis of 1-(4-bromo-1-hydroxynaphthalen-2-yl)-ethan-1-one(2)

1-(4- Bromo -1-hydroxynaphthalen-2-yl)-ethan-1-one was prepared by modified Nenchis Method in which 4- bromo -naphthalen-1-ol was refluxed with glacial acetic acid in presence of fused $ZnCl_2$.

Synthesis of 1-(4- bromo -1-hydroxynaphthalen-2-yl)-3-aryl-prop-2-en-1-one(3-6)

1-(4- Bromo -1-hydroxynaphthalen-2yl)-3-aryl-prop-2-en-1-one were synthesized from 1-(4-bromo -1-hydroxynaphthalen-2-yl)-ethan-1-one by condensing it with aromatic aldehydes.

Synthesis of 4-(4-bromo-1-hydroxynaphthalen-2-yl)-6-aryl-5,6-dihydropyrimidin-2(1H)-one(7-10)

1-(4-Bromo-1-hydroxynaphthalen-2-yl)-3-aryl-prop-2-en-1-ones, urea and concentrated HCl in DMF were added and refluxed for 8 Hours. Cool & pour in crushed ice It was then treated with cold NH_4OH Solution to get 4-(4-bromo-1-hydroxynaphthalen-2-yl)-6-aryl-5,6-dihydropyrimidin-2(1H)-one.

SCHEME

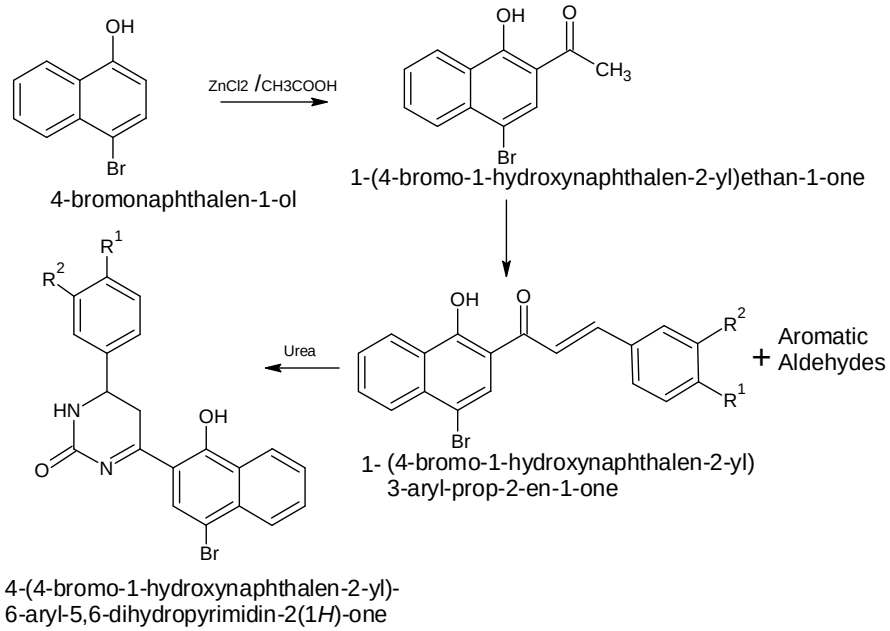

Table 1: Physical Data of Synthesized Compounds.

Sr.No.	Compound No	R_1	R_2	Molecular formula	Melting Point ^{0}C	% Yield	% Nitrogen		R.F. Value
							Found	Calculated	
1	3	$-OCH_3$	-H	--	125^{0}C	57%	--	--	--
2	4	$-OCH_3$	$-OCH_3$	--	129^{0}C	61%	--	--	--
3	5	-H	-OH	--	141^{0}C	58%	--	--	--
4	6	-OH	-H	--	137^{0}C	54%	--	--	--
9	7	$-OCH_3$	-H	C21H17BrN2O3	257^{0}C	43%	6.60	6.59	0.58
10	8	$-OCH_3$	$-OCH_3$	C22H19BrN2O4	217^{0}C	47%	6.19	6.16	0.65
11	9	-H	-OH	C20H15BrN2O3	225^{0}C	42%	6.85	6.81	0.52
12	10	-OH	-H	C20H15BrN2O3	267^{0}C	47%	6.83	6.81	0.53

Spectral Analysis: Spectral interpretation of (8)

IR (ν_{max}) (cm^{-1}) : 1705 (C=O, str), 3351 (NH_2, str), 2950 (CH aliphatic) , 3225 (NH, bend), 1172 (C-O-C str), 1169 (C-O-C str)

NMR (δ ppm): 1.3-1.8 (m, 2H, $-CH_2$ of pyrimidine), 3.7 (s, 3H, $-OCH_3$), 3.9 (s, 3H, $-OCH_3$), 4.3 (t, 1H, CH of pyramidine),5.6 (s, 1H, NH exchangeable with D2O) , 7.1 – 8.9 (m, 9H, Ar-H)

Antimicrobial Studies

Above synthesized 4-(4-bromo-1-hydroxynaphthalen-2-YL)-6-aryl-5,6-dihydropyrimidin-2(1H)-ones have been studied for their antimicrobial activity against Escherichia coli, Proteus mirabilis, Staphylococcus aureas, Pseudomonas aeruginosa. The culture of each

species was incubated at 37^0C and the zone of inhibition was measured after 24 hr. Most of these compounds were found active.

Sr. No.	Compound Number	Antimicrobial activity			
		E-coli	Proteus mirabilis	Staphylococcus aureas	Pseudomonas aeruginosa
1	7	14	10	13	11
2	8	12	11	08	14
3	9	10	09	18	18
4	10	13	12	12	13

Strongly active, range 15-18 Weakly active, range 7-10 mm

Moderately active, range 11-14mm Inactive, -

Thus from above results it was observed that these heterocyclic compounds were found effective against *Escherichia coli, Proteus mirabilis, Staphylococcus aureas, Pseudomonas aeruginosa*. So those compounds can be easily be used for the treatment of diseases caused by test pathogens, only when they does not have toxic and other side effects.

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